



## Clinical trial results:

**ACcomplish: A Phase 2, multicenter, double-blind, randomized, placebo-controlled, dose escalation trial evaluating safety, efficacy, and pharmacokinetics of subcutaneous doses of TransCon CNP administered once weekly for 52 weeks in prepubertal children with achondroplasia followed by an Open-Label Extension Period**

### Summary

EudraCT number	2019-002754-22
Trial protocol	IE GB DE AT DK PT
Global end of trial date	01 October 2024

### Results information

Result version number	v2 (current)
This version publication date	24 May 2025
First version publication date	11 April 2023
Version creation reason	<ul style="list-style-type: none"><li>New data added to full data set update to include OLE safety data</li></ul>

### Trial information

#### Trial identification

Sponsor protocol code	TCC-201
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04085523
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Ascendis Pharma Growth Disorders A/S
Sponsor organisation address	Tuborg Blvd 12, Hellerup, Denmark, DK 2900
Public contact	Clinical Trial Information Desk, Ascendis Pharma A/S, 0045 70222244, clinhelpdesk@ascendispharma.com
Scientific contact	Clinical Trial Information Desk, Ascendis Pharma A/S, 0045 70222244, clinhelpdesk@ascendispharma.com

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 February 2025
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 October 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

In prepubertal children with achondroplasia (ACH) at 52 weeks

- To determine the safety of once weekly subcutaneous (SC) doses of TransCon CNP
- To evaluate the effect of once weekly SC doses of TransCon CNP on annualized height velocity (AHV).

Protection of trial subjects:

Written informed consent was obtained from all subjects prior to enrollment into the trial, as dictated by the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	New Zealand: 2
Country: Number of subjects enrolled	United States: 29
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Denmark: 6
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Ireland: 6
Worldwide total number of subjects	57
EEA total number of subjects	17

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	57
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Overall, 57 subjects were enrolled and dosed. Enrollment of subjects occurred in eight countries: Australia, Austria, Denmark, Germany, Ireland, Portugal, New Zealand, and the United States.

### Pre-assignment

Screening details:

A total of 60 subjects were screened and 57 of these met eligibility criteria and were enrolled into the study. All 57 subjects completed the 52-week double-blind period and entered the 104-week open-label extension (OLE), where they received TransCon CNP. All subjects received up to a maximum dose level of 100-mcg dose of TransCon CNP during OLE.

### Period 1

Period 1 title	52 Week Blinded Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	TransCon CNP (6 mcg/kg/wk)

Arm description:

Once weekly subcutaneous administration of TransCon CNP 6 mcg CNP/kg/week.

Arm type	Experimental
Investigational medicinal product name	TransCon CNP
Investigational medicinal product code	ACP-015
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

TransCon CNP 3.9 mg CNP-38/vial drug product is a lyophilized powder in a single-use glass vial. Prior to use, the lyophilizate is reconstituted with sterile water for injection from a prefilled syringe.

<b>Arm title</b>	TransCon CNP (20 mcg/kg/wk)
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Arm description:

Once weekly subcutaneous administration of TransCon CNP 20 mcg CNP/kg/week.

Arm type	Experimental
Investigational medicinal product name	TransCon CNP
Investigational medicinal product code	ACP-015
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

TransCon CNP 3.9 mg CNP-38/vial drug product is a lyophilized powder in a single-use glass vial. Prior to use, the lyophilizate is reconstituted with sterile water for injection from a prefilled syringe.

<b>Arm title</b>	TransCon CNP (50 mcg/kg/wk)
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Arm description:

Once weekly subcutaneous administration of TransCon CNP 50 mcg CNP/kg/week.

Arm type	Experimental
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Investigational medicinal product name	TransCon CNP
Investigational medicinal product code	ACP-015
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

TransCon CNP 3.9 mg CNP-38/vial drug product is a lyophilized powder in a single-use glass vial. Prior to use, the lyophilizate is reconstituted with sterile water for injection from a prefilled syringe.

<b>Arm title</b>	TransCon CNP (100 mcg/kg/wk)
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Arm description:

Once weekly subcutaneous administration of TransCon CNP 100 mcg CNP/kg/week.

Arm type	Experimental
Investigational medicinal product name	TransCon CNP
Investigational medicinal product code	ACP-015
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

TransCon CNP 3.9 mg CNP-38/vial drug product is a lyophilized powder in a single-use glass vial. Prior to use, the lyophilizate is reconstituted with sterile water for injection from a prefilled syringe.

<b>Arm title</b>	Pooled Placebo
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Arm description:

Once weekly subcutaneous administration of placebo for TransCon CNP to mimick the dose (6, 20, 50, or 100 mcg/kg/week) of investigational product.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo for TransCon CNP is a lyophilized powder in a single-use glass vial. Prior to use, the lyophilizate is reconstituted with sterile water for injection from a prefilled syringe.

<b>Number of subjects in period 1</b>	TransCon CNP (6 mcg/kg/wk)	TransCon CNP (20 mcg/kg/wk)	TransCon CNP (50 mcg/kg/wk)
Started	10	11	10
Completed	10	11	10

<b>Number of subjects in period 1</b>	TransCon CNP (100 mcg/kg/wk)	Pooled Placebo
Started	11	15
Completed	11	15

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**Period 2**

Period 2 title	Open-Label Period (Weeks 52 to 156)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

**Arms**

<b>Arm title</b>	Open-Label Extension Period: TransCon CNP
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## Arm description:

Subjects who completed the 52-week blinded treatment period continued into the 104-week open-label extension period and received treatment with TransCon CNP (navepegritide) doses escalated up to a maximum of 100 mcg/kg delivered once weekly by subcutaneous injection.

Arm type	Experimental
Investigational medicinal product name	TransCon CNP
Investigational medicinal product code	ACP-015
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

## Dosage and administration details:

TransCon CNP 3.9 mg CNP-38/vial drug product is a lyophilized powder in a single-use glass vial. Prior to use, the lyophilizate is reconstituted with sterile water for injection from a prefilled syringe.

<b>Number of subjects in period 2</b>	Open-Label Extension Period: TransCon CNP
Started	57
Completed	55
Not completed	2
Consent withdrawn by subject	2

## Baseline characteristics

### Reporting groups

Reporting group title	TransCon CNP (6 mcg/kg/wk)
Reporting group description: Once weekly subcutaneous administration of TransCon CNP 6 mcg CNP/kg/week.	
Reporting group title	TransCon CNP (20 mcg/kg/wk)
Reporting group description: Once weekly subcutaneous administration of TransCon CNP 20 mcg CNP/kg/week.	
Reporting group title	TransCon CNP (50 mcg/kg/wk)
Reporting group description: Once weekly subcutaneous administration of TransCon CNP 50 mcg CNP/kg/week.	
Reporting group title	TransCon CNP (100 mcg/kg/wk)
Reporting group description: Once weekly subcutaneous administration of TransCon CNP 100 mcg CNP/kg/week.	
Reporting group title	Pooled Placebo
Reporting group description: Once weekly subcutaneous administration of placebo for TransCon CNP to mimick the dose (6, 20, 50, or 100 mcg/kg/week) of investigational product.	

Reporting group values	TransCon CNP (6 mcg/kg/wk)	TransCon CNP (20 mcg/kg/wk)	TransCon CNP (50 mcg/kg/wk)
Number of subjects	10	11	10
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	6.52 ± 2.593	6.29 ± 2.896	5.20 ± 2.991
Gender categorical Units: Subjects			
Female	7	3	3
Male	3	8	7
Race Units: Subjects			
American Indian or Alaskan Native	0	0	0
Asian	2	1	1
Black or African American	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	1
White	8	10	8
Other	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	2
Not Hispanic or Latino	9	11	6
Unknown/Not Reported	0	0	2
Region Units: Subjects			

North America	4	4	4
Europe	2	5	4
Oceania	4	2	2
Height			
Units: cm			
arithmetic mean	90.63	92.29	86.61
standard deviation	± 8.973	± 12.103	± 12.967
Height SDS			
Units: Standard deviation score (SDS)			
arithmetic mean	-5.45	-4.87	-4.85
standard deviation	± 1.046	± 0.673	± 0.801
Weight			
Units: kg			
arithmetic mean	17.49	19.67	15.67
standard deviation	± 3.677	± 6.602	± 4.399
Body Mass Index			
Units: kg^m2			
arithmetic mean	21.10	22.52	20.61
standard deviation	± 1.664	± 2.599	± 1.496
Baseline AHV			
Baseline annualized height velocity (AHV)			
Units: cm/year			
arithmetic mean	5.04	5.29	5.76
standard deviation	± 2.157	± 1.619	± 3.147

<b>Reporting group values</b>	TransCon CNP (100 mcg/kg/wk)	Pooled Placebo	Total
Number of subjects	11	15	57
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	5.79	5.89	
standard deviation	± 2.613	± 3.109	-
Gender categorical			
Units: Subjects			
Female	6	5	24
Male	5	10	33
Race			
Units: Subjects			
American Indian or Alaskan Native	0	0	0
Asian	0	2	6
Black or African American	1	1	2
Native Hawaiian or Other Pacific Islander	0	0	1
White	10	12	48
Other	0	0	0
Ethnicity			
Units: Subjects			
Hispanic or Latino	2	1	6
Not Hispanic or Latino	9	14	49



Unknown/Not Reported	0	0	2
Region			
Units: Subjects			
North America	8	9	29
Europe	3	3	17
Oceania	0	3	11
Height			
Units: cm			
arithmetic mean	89.23	90.85	
standard deviation	± 12.822	± 14.920	-
Height SDS			
Units: Standard deviation score (SDS)			
arithmetic mean	-4.92	-4.85	
standard deviation	± 0.829	± 0.958	-
Weight			
Units: kg			
arithmetic mean	17.03	17.99	
standard deviation	± 4.699	± 5.542	-
Body Mass Index			
Units: kg^m2			
arithmetic mean	21.11	21.39	
standard deviation	± 1.612	± 1.853	-
Baseline AHV			
Baseline annualized height velocity (AHV)			
Units: cm/year			
arithmetic mean	4.73	6.17	
standard deviation	± 1.133	± 1.394	-

## End points

### End points reporting groups

Reporting group title	TransCon CNP (6 mcg/kg/wk)
Reporting group description: Once weekly subcutaneous administration of TransCon CNP 6 mcg CNP/kg/week.	
Reporting group title	TransCon CNP (20 mcg/kg/wk)
Reporting group description: Once weekly subcutaneous administration of TransCon CNP 20 mcg CNP/kg/week.	
Reporting group title	TransCon CNP (50 mcg/kg/wk)
Reporting group description: Once weekly subcutaneous administration of TransCon CNP 50 mcg CNP/kg/week.	
Reporting group title	TransCon CNP (100 mcg/kg/wk)
Reporting group description: Once weekly subcutaneous administration of TransCon CNP 100 mcg CNP/kg/week.	
Reporting group title	Pooled Placebo
Reporting group description: Once weekly subcutaneous administration of placebo for TransCon CNP to mimic the dose (6, 20, 50, or 100 mcg/kg/week) of investigational product.	
Reporting group title	Open-Label Extension Period: TransCon CNP
Reporting group description: Subjects who completed the 52-week blinded treatment period continued into the 104-week open-label extension period and received treatment with TransCon CNP (navepegritide) doses escalated up to a maximum of 100 mcg/kg delivered once weekly by subcutaneous injection.	

### Primary: Annualized Height Velocity

End point title	Annualized Height Velocity
End point description: The primary efficacy analysis compared the difference in the primary efficacy endpoint between the TransCon CNP treatment group and the pooled placebo group using an ANCOVA model with the annualized height velocity (AHV) at Week 52 as the response variable, treatment (TransCon CNP dose groups and placebo) and sex as factors, baseline age and baseline height SDS as the covariates, and based on the Full Analysis Set.	
End point type	Primary
End point timeframe: 52 weeks	

End point values	TransCon CNP (6 mcg/kg/wk)	TransCon CNP (20 mcg/kg/wk)	TransCon CNP (50 mcg/kg/wk)	TransCon CNP (100 mcg/kg/wk)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	10	11
Units: cm/year				
least squares mean (confidence interval 95%)	4.09 (3.34 to 4.84)	4.52 (3.82 to 5.22)	5.16 (4.43 to 5.90)	5.42 (4.74 to 6.11)

<b>End point values</b>	Pooled Placebo			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: cm/year				
least squares mean (confidence interval 95%)	4.35 (3.75 to 4.94)			

## Statistical analyses

<b>Statistical analysis title</b>	Primary efficacy endpoint
Statistical analysis description: ANCOVA model using treatment (dose groups and pooled placebo) and sex as fixed effects, and baseline age and baseline height SDS as the covariates.	
Comparison groups	TransCon CNP (6 mcg/kg/wk) v Pooled Placebo
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6004
Method	ANCOVA

<b>Statistical analysis title</b>	Primary efficacy endpoint
Statistical analysis description: ANCOVA model using treatment (dose groups and pooled placebo) and sex as fixed effects, and baseline age and baseline height SDS as the covariates.	
Comparison groups	TransCon CNP (20 mcg/kg/wk) v Pooled Placebo
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7022
Method	ANCOVA

<b>Statistical analysis title</b>	Primary efficacy endpoint
Statistical analysis description: ANCOVA model using treatment (dose groups and pooled placebo) and sex as fixed effects, and baseline age and baseline height SDS as the covariates.	
Comparison groups	TransCon CNP (50 mcg/kg/wk) v Pooled Placebo
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0849
Method	ANCOVA

<b>Statistical analysis title</b>	Primary efficacy endpoint
Statistical analysis description: ANCOVA model using treatment (dose groups and pooled placebo) and sex as fixed effects, and baseline age and baseline height SDS as the covariates.	
Comparison groups	TransCon CNP (100 mcg/kg/wk) v Pooled Placebo
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0218
Method	ANCOVA

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From Week 0 to Week 52 for double-blind treatment period and up to Week 156 for OLE Period

Adverse event reporting additional description:

Analysis was performed on safety analysis set that included all randomised subjects who received at least one dose of trial drug. Subjects were analysed according to trial treatment as treated. Adverse Events were reported as per MedDRA version 24.1 for double-blind treatment period and MedDRA version 26.0 for OLE period.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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### Reporting groups

Reporting group title	TransCon CNP (6 mcg/kg/wk)
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Reporting group description:

Once weekly subcutaneous administration of TransCon CNP 6 mcg CNP/kg/week.

Reporting group title	TransCon CNP (20 mcg/kg/wk)
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Reporting group description:

Once weekly subcutaneous administration of TransCon CNP 20 mcg CNP/kg/week.

Reporting group title	TransCon CNP (50 mcg/kg/wk)
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Reporting group description:

Once weekly subcutaneous administration of TransCon CNP 50 mcg CNP/kg/week.

Reporting group title	TransCon CNP (100 mcg/kg/wk)
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Reporting group description:

Once weekly subcutaneous administration of TransCon CNP 100 mcg CNP/kg/week.

Reporting group title	Pooled Placebo
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Reporting group description:

Once weekly subcutaneous administration of placebo for TransCon CNP to mimick the dose (6, 20, 50, or 100 mcg/kg/week) of investigational product.

Reporting group title	Open-Label Extension Period: TransCon CNP
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Reporting group description:

Subjects who completed the 52-week blinded treatment period continued into the 104-week open-label extension period and received treatment with TransCon CNP (navepegitide) doses escalated up to a maximum of 100 mcg/kg delivered once weekly by subcutaneous injection.

Serious adverse events	TransCon CNP (6 mcg/kg/wk)	TransCon CNP (20 mcg/kg/wk)	TransCon CNP (50 mcg/kg/wk)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Febrile convulsion			

subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Obstructive sleep apnoea syndrome alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar hypertrophy			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Viral infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	TransCon CNP (100 mcg/kg/wk)	Pooled Placebo	Open-Label Extension Period: TransCon CNP
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	2 / 57 (3.51%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Febrile convulsion			

subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Obstructive sleep apnoea syndrome			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar hypertrophy			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	TransCon CNP (6 mcg/kg/wk)	TransCon CNP (20 mcg/kg/wk)	TransCon CNP (50 mcg/kg/wk)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)	11 / 11 (100.00%)	10 / 10 (100.00%)
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2	4 / 11 (36.36%) 7	2 / 10 (20.00%) 2
Injection site reaction subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 11 (9.09%) 1	1 / 10 (10.00%) 1
Fatigue subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	2 / 11 (18.18%) 2	0 / 10 (0.00%) 0
Influenza like illness alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0
Injection site pain alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0
Injection site swelling alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	1 / 10 (10.00%) 1
Immune system disorders Seasonal allergy alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	4 / 10 (40.00%) 7	3 / 11 (27.27%) 7	4 / 10 (40.00%) 6
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	2 / 11 (18.18%) 2	2 / 10 (20.00%) 4
Nasal congestion subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	3 / 11 (27.27%) 4	2 / 10 (20.00%) 3



Epistaxis			
subjects affected / exposed	1 / 10 (10.00%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	1	2	1
Oropharyngeal pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	3
Snoring			
subjects affected / exposed	1 / 10 (10.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Obstructive sleep apnoea syndrome			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Tonsillar hypertrophy			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
Vitamin D decreased			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Skin abrasion			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	3 / 10 (30.00%) 4
Blood and lymphatic system disorders Lymphadenopathy alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)  Hypoacusis alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)  Middle ear effusion alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1  0 / 10 (0.00%) 0  0 / 10 (0.00%) 0	1 / 11 (9.09%) 1  0 / 11 (0.00%) 0  0 / 11 (0.00%) 0	1 / 10 (10.00%) 1  1 / 10 (10.00%) 1  1 / 10 (10.00%) 1
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)  Diarrhoea subjects affected / exposed occurrences (all)  Abdominal pain upper subjects affected / exposed occurrences (all)  Abdominal pain alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)  Nausea alternative dictionary used:	1 / 10 (10.00%) 1  1 / 10 (10.00%) 1  0 / 10 (0.00%) 0  0 / 10 (0.00%) 0  0 / 10 (0.00%) 0	2 / 11 (18.18%) 4  0 / 11 (0.00%) 0  1 / 11 (9.09%) 1  1 / 11 (9.09%) 1	2 / 10 (20.00%) 3  2 / 10 (20.00%) 3  1 / 10 (10.00%) 1  0 / 10 (0.00%) 0

MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 10 (10.00%)	1 / 11 (9.09%)	3 / 10 (30.00%)
occurrences (all)	1	1	7
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	3 / 10 (30.00%)
occurrences (all)	1	0	4
Back pain			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Knee deformity			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 10 (30.00%)	1 / 11 (9.09%)	5 / 10 (50.00%)
occurrences (all)	3	1	8
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	5 / 10 (50.00%)
occurrences (all)	2	0	6
Gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 11 (18.18%)	3 / 10 (30.00%)
occurrences (all)	0	2	3
COVID-19			

subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Otitis media			
subjects affected / exposed	1 / 10 (10.00%)	2 / 11 (18.18%)	2 / 10 (20.00%)
occurrences (all)	1	2	2
Viral infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	2	4
Respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	3 / 10 (30.00%)
occurrences (all)	0	0	5
Conjunctivitis			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ear infection			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gastroenteritis viral			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Influenza			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 10 (10.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Otitis media acute			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 10 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pharyngitis			
alternative dictionary used: MedDRA 26.0			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0
Pharyngitis streptococcal alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0
Rhinitis alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 11 (9.09%) 1	1 / 10 (10.00%) 1
Sinusitis alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0
Viral upper respiratory tract infection alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 11 (0.00%) 0	0 / 10 (0.00%) 0
Metabolism and nutrition disorders Vitamin D deficiency subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 11 (9.09%) 1	0 / 10 (0.00%) 0

<b>Non-serious adverse events</b>	TransCon CNP (100 mcg/kg/wk)	Pooled Placebo	Open-Label Extension Period: TransCon CNP
Total subjects affected by non-serious adverse events subjects affected / exposed	10 / 11 (90.91%)	14 / 15 (93.33%)	57 / 57 (100.00%)
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 4	5 / 15 (33.33%) 8	23 / 57 (40.35%) 56
Injection site reaction subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 2	1 / 15 (6.67%) 1	5 / 57 (8.77%) 24
Fatigue			

subjects affected / exposed	0 / 11 (0.00%)	1 / 15 (6.67%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	3 / 57 (5.26%)
occurrences (all)	0	0	3
Injection site pain			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	6 / 57 (10.53%)
occurrences (all)	0	0	26
Injection site swelling			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	4 / 57 (7.02%)
occurrences (all)	0	0	6
Immune system disorders			
Seasonal allergy			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	1 / 11 (9.09%)	0 / 15 (0.00%)	6 / 57 (10.53%)
occurrences (all)	1	0	8
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 11 (18.18%)	3 / 15 (20.00%)	21 / 57 (36.84%)
occurrences (all)	4	5	51
Rhinorrhoea			
subjects affected / exposed	2 / 11 (18.18%)	1 / 15 (6.67%)	11 / 57 (19.30%)
occurrences (all)	2	1	18
Nasal congestion			
subjects affected / exposed	0 / 11 (0.00%)	3 / 15 (20.00%)	13 / 57 (22.81%)
occurrences (all)	0	5	31
Epistaxis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	3 / 57 (5.26%)
occurrences (all)	0	0	3
Oropharyngeal pain			
subjects affected / exposed	1 / 11 (9.09%)	2 / 15 (13.33%)	10 / 57 (17.54%)
occurrences (all)	1	2	14

<p>Snoring</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 11 (0.00%)</p> <p>0</p>	<p>3 / 15 (20.00%)</p> <p>3</p>	<p>7 / 57 (12.28%)</p> <p>9</p>
<p>Obstructive sleep apnoea syndrome</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 11 (0.00%)</p> <p>0</p>	<p>0 / 15 (0.00%)</p> <p>0</p>	<p>6 / 57 (10.53%)</p> <p>6</p>
<p>Sleep apnoea syndrome</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 11 (0.00%)</p> <p>0</p>	<p>0 / 15 (0.00%)</p> <p>0</p>	<p>4 / 57 (7.02%)</p> <p>5</p>
<p>Tonsillar hypertrophy</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 11 (0.00%)</p> <p>0</p>	<p>0 / 15 (0.00%)</p> <p>0</p>	<p>3 / 57 (5.26%)</p> <p>3</p>
<p>Investigations</p> <p>Vitamin D decreased</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	<p>0 / 15 (0.00%)</p> <p>0</p>	<p>5 / 57 (8.77%)</p> <p>5</p>
<p>Injury, poisoning and procedural complications</p> <p>Fall</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Skin abrasion</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 11 (0.00%)</p> <p>0</p> <p>0 / 11 (0.00%)</p> <p>0</p>	<p>1 / 15 (6.67%)</p> <p>2</p> <p>0 / 15 (0.00%)</p> <p>0</p>	<p>5 / 57 (8.77%)</p> <p>6</p> <p>3 / 57 (5.26%)</p> <p>3</p>
<p>Nervous system disorders</p> <p>Headache</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 11 (18.18%)</p> <p>2</p>	<p>2 / 15 (13.33%)</p> <p>8</p>	<p>17 / 57 (29.82%)</p> <p>40</p>
Blood and lymphatic system disorders			

Lymphadenopathy alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	0 / 15 (0.00%) 0	4 / 57 (7.02%) 4
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)  Hypoacusis alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)  Middle ear effusion alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0   0 / 11 (0.00%) 0  0 / 11 (0.00%) 0	1 / 15 (6.67%) 1   0 / 15 (0.00%) 0  0 / 15 (0.00%) 0	10 / 57 (17.54%) 22   7 / 57 (12.28%) 10  5 / 57 (8.77%) 6
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)  Diarrhoea subjects affected / exposed occurrences (all)  Abdominal pain upper subjects affected / exposed occurrences (all)  Abdominal pain alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)  Nausea alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	3 / 11 (27.27%) 3   1 / 11 (9.09%) 2  1 / 11 (9.09%) 1  0 / 11 (0.00%) 0  1 / 11 (9.09%) 1	3 / 15 (20.00%) 5   2 / 15 (13.33%) 2  2 / 15 (13.33%) 2  0 / 15 (0.00%) 0  0 / 15 (0.00%) 0	16 / 57 (28.07%) 25   6 / 57 (10.53%) 8  4 / 57 (7.02%) 7  3 / 57 (5.26%) 4  3 / 57 (5.26%) 3
Skin and subcutaneous tissue disorders			



Rash alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 15 (6.67%) 1	4 / 57 (7.02%) 7
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all)  Arthralgia subjects affected / exposed occurrences (all)  Back pain alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)  Knee deformity alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all)	3 / 11 (27.27%) 3  1 / 11 (9.09%) 1  0 / 11 (0.00%) 0  0 / 11 (0.00%) 0	1 / 15 (6.67%) 1  1 / 15 (6.67%) 18  0 / 15 (0.00%) 0  1 / 15 (6.67%) 1	7 / 57 (12.28%) 8  9 / 57 (15.79%) 14  9 / 57 (15.79%) 10  3 / 57 (5.26%) 3
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)  Nasopharyngitis subjects affected / exposed occurrences (all)  Gastroenteritis subjects affected / exposed occurrences (all)  COVID-19 subjects affected / exposed occurrences (all)  Otitis media subjects affected / exposed occurrences (all)  Viral infection	0 / 11 (0.00%) 0  2 / 11 (18.18%) 2  1 / 11 (9.09%) 1  3 / 11 (27.27%) 3  0 / 11 (0.00%) 0	2 / 15 (13.33%) 2  1 / 15 (6.67%) 3  2 / 15 (13.33%) 2  1 / 15 (6.67%) 1  3 / 15 (20.00%) 3	14 / 57 (24.56%) 22  20 / 57 (35.09%) 35  10 / 57 (17.54%) 13  20 / 57 (35.09%) 22  14 / 57 (24.56%) 18

subjects affected / exposed	0 / 11 (0.00%)	2 / 15 (13.33%)	8 / 57 (14.04%)
occurrences (all)	0	3	17
Respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	4 / 57 (7.02%)
occurrences (all)	0	0	5
Ear infection			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	1 / 15 (6.67%)	14 / 57 (24.56%)
occurrences (all)	0	1	27
Gastroenteritis viral			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	2 / 11 (18.18%)	0 / 15 (0.00%)	7 / 57 (12.28%)
occurrences (all)	2	0	11
Influenza			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	10 / 57 (17.54%)
occurrences (all)	0	0	10
Otitis media acute			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	1 / 15 (6.67%)	7 / 57 (12.28%)
occurrences (all)	0	3	15
Pharyngitis			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	5 / 57 (8.77%)
occurrences (all)	0	0	5
Pharyngitis streptococcal			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	5 / 57 (8.77%)
occurrences (all)	0	0	6
Rhinitis			
alternative dictionary used:			

MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	0 / 15 (0.00%)	6 / 57 (10.53%)
occurrences (all)	0	0	6
Sinusitis			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	2 / 11 (18.18%)	0 / 15 (0.00%)	4 / 57 (7.02%)
occurrences (all)	3	0	4
Viral upper respiratory tract infection			
alternative dictionary used: MedDRA 26.0			
subjects affected / exposed	0 / 11 (0.00%)	2 / 15 (13.33%)	6 / 57 (10.53%)
occurrences (all)	0	2	8
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	0 / 11 (0.00%)	1 / 15 (6.67%)	5 / 57 (8.77%)
occurrences (all)	0	1	6

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 September 2020	Protocol Version 2.0 summary of changes: <ul style="list-style-type: none"><li>- increase enrollment to include approximately 14 subjects in Cohorts 2-5</li><li>- add allowance for select visits to be conducted off-site</li><li>- remove BMI as a secondary efficacy endpoint</li><li>- modify the placebo comparator and dosing procedure for Cohort 1</li><li>- add availability of home health nurse to give weekly injections</li><li>- update contact information for SAE reporting</li><li>- update the definition of AE</li></ul>
08 January 2021	Protocol Version 3.0 added a 2 year Open-Label Extension period to assess long term safety and efficacy following the Randomized Period.
12 August 2021	Protocol Version 4.0 added implementation of unblinding per cohort after completion of the Randomized Treatment Period.
28 December 2022	Protocol Version 5.0 summary of changes: <ul style="list-style-type: none"><li>- Added information of a new separate long-term open-label extension study for subjects completing treatment in the TCC-201 protocol</li><li>- Updated SAE reporting</li></ul>

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported